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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/016,177	10/25/2001	Kevin P. Baker	GNE.2630P1C90	4438

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EXAMINER	
SAOUD, CHRISTINE J	
ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 09/21/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/016,177	BAKER ET AL.	
	Examiner	Art Unit	
	Christine J. Saoud	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *58-65,68-70 and 74-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *58-65,69,70 and 74-77* is/are rejected.

7)☒ Claim(s) *68* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *6/22/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 58-62 have been amended in the paper filed 22 June 2005. Claims 58-65, 68-70 and 74-77 are pending in the instant application.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Any objection or rejection of record which is not expressly repeated in this action has been overcome by Applicant's response and withdrawn.

Applicant's arguments filed 22 June 2005 have been fully considered but are not persuasive.

Information Disclosure Statement

Applicant's IDS filed 22 June 2005 has been received and considered.

Priority

As indicated in the previous Office actions and reiterated by Applicant in the response of 22 December 2004, the instant application has been granted priority based on the fetal hemoglobin induction assay which was first disclosed in PCT/US00/04341, which was filed February 18, 2000. All prior art rejections are based on this priority date.

Claim Rejections - 35 USC § 102

Claims 58-61, 74-77 stand rejected under 35 U.S.C. 102(e) as being anticipated by Parham et al. (U.S. Pat. No. 6,586,228) for the reasons of record and for those reasons provided below.

Applicant argues at page 7 of the response that molecule of Parham et al. is only 1381 nucleotides in length and that the molecule of SEQ ID NO:351 is 2056 nucleotides in length. Applicant argues that the nucleic acid of Parham et al. only has 67.6% identity to the entire length of SEQ ID NO:351, and therefore, Parham et al. does not meet the limitations of the claims. Applicant's arguments have been fully considered but are not persuasive.

Note the specification sets for the following definition on page 123, lines 24-28:

"Percent (%) amino acid sequence identity" with respect to the PRO polypeptide sequences identified herein is defined as **the percentage of amino acid residues in a candidate sequence that are identical with the amino acid residues in the specific PRO polypeptide sequence**, after aligning the sequences and introducing gaps, if necessary, to achieve the maximum percent sequence identity, and not considering any conservative substitutions as part of the sequence identify.

Based on this definition in the specification and no limitation in the claim that the comparison is to be made to the entire length of SEQ ID NO:351, the percentage of nucleotides in the candidate sequence that are identical to the nucleotides in the PRO molecule is calculated as 98.1%. Therefore, Parham et al. meets the structural limitations of the claims. Since the structural limitations are met, one ordinary skill in the art would expect the functional limitations to also be met even though Parham et al. is silent to the biological activity of the disclosed molecule in the MLR assay, absent

evidence to the contrary. Applicant should note that an argument to the contrary may serve as the basis of an enablement rejection of the claims.

Claims 58-65, 69-70, 74-77 stand rejected under 35 U.S.C. 102(e) as being anticipated by Thompson et al. (U.S. Pat. No. 6,610,286).

Applicant argues the rejections over Thompson et al. by noting that the claims have been amended to recite that the encoded polypeptide inhibits T-cell proliferation in the MLR assay. Applicant claims priority to provisional application 60/087,106, filed on May 28, 1998 based on the ability of the encoded PRO protein to inhibit T-cell proliferation in the MLR assay. Applicant asserts that the ability of PRO1114 to inhibit T-cell proliferation in the MLR assay supports a utility in "therapeutical applications when inhibition of the immune response is desired, such as in autoimmune diseases or in graft rejection". Applicant's arguments have been fully considered, but are not persuasive.

The specification at page 354 states "[c]ompounds which inhibit proliferation of lymphocytes are useful therapeutically where suppression of an immune response is beneficial" and "[a]ny value less than control indicates an inhibitory effect for the test protein" (lines 10-11 and 36-37, respectively). However, the ability of a protein to stimulate lymphocyte proliferation in this assay does not support a specific and substantial utility for the claimed invention for the reasons that follow.

The ability to stimulate or inhibit lymphocyte proliferation in the MLR assay is an artificial *in vitro* system and does not provide for what specific conditions or for which specific diseases the claimed invention would predictably function. The assertion that the claimed invention could be useful for the treatment of conditions where the enhancement of the immune response would be beneficial (page 354) is not specific since there are many such conditions, and it is not predictable of which conditions the claimed invention may function, if any. Secondly, the ability to stimulate lymphocytes in the MLR assay does not provide for a substantial utility because the MLR assay is not predictive of the ability of a molecule to suppress an immune response *in vivo,* as asserted in the specification, and further significant experimentation would be required to reasonable confirm this asserted utility.

Mixed lymphocyte culture (MLC) is a special case of antigen stimulation in which T lymphocytes respond to foreign histocompatibility antigen on unrelated lymphocytes or monocytes. MLC is a functional assay of cellular response to stimulatory determinants associated predominantly with HLA class II molecules. A single genetic locus or region, known as HLA, controls the MLC reactivity. The MLC assay recognizes disparate HLA class II molecules and the resulting T-cell activation, which is thought to represent an *in vitro* model of the afferent arm of the *in vivo* allograft reaction. The degree of reactivity observed correlates with the degree of antigenic disparity between responding and stimulating cells. Briefly, when the lymphocytes of 2 HLA-disparate individuals are combined in tissue culture, the cells enlarge, synthesize DNA, and proliferate, whereas HLA-identical cells remain quiescent. Since both cells will normally

proliferate, a one way test is used to monitor the response of a single responder cell by inactivating the stimulator cell by radiation or drugs in order to inhibit DNA synthesis of the stimulator cell. The proliferation is driven primarily by the differences in the class II HLA antigens between the 2 test cells (or individuals). This reaction is not predictive of general responses of the immune system because, *in vivo*, activation of a lymphocyte is controlled not only by antigen binding but also by interactions with other cells. All T cells must cooperate with antigen-presenting cells, whereas B cells and cytotoxic T cells depend on helper T lymphocytes. These interactions either require direct surface-to surface contact or are mediated by cytokines that act only over extremely short distances. Because of this interdependence, lymphocyte activation occurs commonly and efficiently in the secondary lymphoid organs, where lymphocytes, antigens, and antigen-presenting cells encounter one another at close quarters. See pages 30-31, 208-209, 246-247 of "Basic and Clinical Immunology", 1994. See also, "Manual of Clinical Laboratory Immunology", 6th Edition at pages 1164-1166.

Kahan clearly states that no *in vitro* immune assay predicts or correlates with *in vivo* immunosuppressive efficacy; there is no surrogate immune parameter as a basis of immunosuppressive efficacy and/or for dose extrapolation from *in vitro* systems to *in vivo* conditions (Cur. Opin. Immunol. 4: 553-560, 1992; see entire document, particularly page 558, column 2). Piccotti et al. (Transplantation 67: 1453-1460, 1999) demonstrate that IL-12 enhances alloantigen-specific immune function as determined by MLC, but this result *in vitro* does not result in a measurable response *in vivo* (i.e. failure to accelerate allograft rejection) (see page 1459). Campo et al. (Biological Trace

Element Res. 79: 15-22, 2001) demonstrate that while zinc suppresses alloreactivity in MLC, it does not decrease T-cell proliferation *in vitro* nor produce immunosuppressive effects *in vivo*. Therefore, the MLC assay, which is art recognized for determining histocompatibility, does not appear to be predictive of general immune responses *in vivo*.

Additionally, difficulties arise in quantification when using MLC as a test for T cell function due to variations in stimulator cell antigens that determine the degree of genetic disparity between stimulator and responder cells. MLC is typically used for determining histocompatibilty in an individual and as a test for immunocompetence of T cells in patients with immunodeficiency disorders. When running the MLC assay for determining histocompatibility for transplantation, autologous controls combining self with irradiated self are necessary to normalize the response of each cell to stimulators. Furthermore, there is known inherent variability of individual cellular responses from day to day which requires performing the entire familial MLC at one time in the case of determining histocompatibility for transplantation (page 246 in "Basic and Clinical Immunology"). When performing the MLC assay, each individual lot of a serum source should be screened for growth support capabilities and possible HLA antibodies (see page 1165 in "Manual of Clinical Laboratory Immunology"). Additionally, the screen should include a control response to a pool of allogeneic cells to measure maximum response and an autologous control to ensure low backgrounds. Such controls appear to be lacking in the instant specification.

Therefore, the MLC (a.k.a. MLR) assay is a measure of alloreactivity of one individual to another individual, rather than a general measure of immune function. This reactivity is governed by the antigenic disparity between the two individuals which are being compared in the assay. Depending on the individuals being tested, the MLC may indicate stimulation if they are HLA-disparate or the MLC may indicate no stimulation if the individuals are HLA-identical. The ability of the claimed invention to stimulate proliferation in the MLC assay may not be a general stimulus to lymphocyte proliferation, but rather a reaction to one of the MHC antigens on the responder cell. The instant specification fails to provide sufficient detail of the assay which was performed and fails to provide any data whatsoever in order for one of ordinary skill in the art to evaluate the conclusion that lymphocyte proliferation was stimulated by the claimed invention. As pointed out above, there are several controls which the art recognizes as being essential for meaningful results for this assay, including autologous controls, a control to determine maximum response, screening for possible HLA antibodies and growth support capabilities. Furthermore, there is known inherent variability of individual cellular responses from day to day, which would clearly dictate the need for internal controls. The specification indicates that CD4-IgG was used as a control, but it is not clear how this would control for background stimulation or provide for a measure of maximal stimulation. Lastly, the specification fails to provide any data or evidence of the results of the assay, therefore, one of ordinary skill in the art cannot evaluate the conclusion. The specification states that "positive increases over control are considered positive", however, this does not indicate that statistical significance

must occur for determination of a positive result in the assay. In conclusion, the results of the MLC (a.k.a. MLR) assay do not support a specific and substantial utility for the claimed invention because the assay is not predictive of immune response in general, and one of ordinary skill in the art would not expect a stimulatory effect in the MLC assay to correlate to a general stimulatory effect on the immune system, absent evidence to the contrary.

The Declaration filed on 22 June 2005 under 37 CFR 1.131 has been considered but is ineffective to overcome the Thompson et al. reference.

The Declaration states that Applicant had cloned and sequenced the molecule PRO1114 and had identified its homology to cytokine receptor family proteins. The Declaration also states that Applicant had tested PRO1114 in the MLR assay prior to the date of December 23, 1999, as evidenced by Exhibit A. First, Exhibit A is illegible and no meaningful interpretation of what is being evidenced can be made. Secondly, although the provisional application identified homology of the claimed invention to cytokine receptor proteins, this structural similarity is not sufficient to provide a specific and substantial credible utility for the claimed invention. "Cytokines ... represent a bewildering array of different molecules with sometimes puzzling sets of biological activities which often overlap with each other." (see page 1 of Guidebook to Cytokines and Their Receptors at column 2, 2nd full paragraph, first sentence). The claimed invention has homology to cytokine receptors, which is also a large, diverse, collection of proteins which bind different cytokines in order to mediate the biological activities possessed, which include proliferation and/or differentiation of immunohemopoietic

cells, immune regulation, antiviral effects, pleiotropic effects on the liver, fat cells, nerves, muscle, macrophages, hormone regulation, cytokine synthesis, growth inhibition, tissue modeling, growth of epithelial cells and endothelial cells, survival/growth/differentiation of nerve cells, mediation of cell death, etc. (see pages 4-5 of Guidebook to Cytokines and Their Receptors). The biological activity of the receptor depends on the ligand that binds the receptor, which cannot be determined from structural similarity to other cytokine receptors. Therefore, the knowledge of homology to cytokine receptors is not sufficient to provide a specific or substantial utility for the claimed invention because without knowing the biological effects mediated by the receptor or the ligand that binds the receptor, one of ordinary skill in the art would not know how to use the invention.

It is noted that the Declaration is not signed and no signed copy has been received as of the date of the instant office action.

At page 9 of the response, Applicant argues that Thompson et al. suggest treatment of inflammation and inflammatory diseases with the protein of SEQ ID NO:14. Applicant "submit that the results of the MLR assay demonstrate a comparable utility for PRO1114" when inhibition of the immune response is desired. Applicant's argument has been fully considered, but is not persuasive. As was pointed out above, the MLR assay is not predictive of general immune responses in vivo, and likewise, is not predictive of treatment of inflammation for the same reasons. Furthermore, an assertion of inhibition of the immune response is not a specific disclosure of treatment of

inflammation and inflammatory diseases. Disclosure of a genus does not necessarily provide a basis for the species, as is the current assertion.

Applicant asserts that the MLR assay is well-described in textbooks, which is not a point of dispute. The assay may be well-known, but the conclusion which is drawn from this assay is not that a molecule would be useful for inhibition of an immune response in an individual if it tests positive in this assay. The references provided above support the position that the MLR assay is not predictive of general immune responses *in vivo*, but is art recognized for determining histocompatibility, among other things. The Examiner has not found art to support Applicant's position that the MLR assay is predictive of immune responses in general. Further complicating the matter is that the information provided in the specification is so sparse regarding the MLR assay and the data obtained from which the conclusion that PRO1114 was an inhibitory compound, one of ordinary skill in the art cannot evaluate the data because none is provided and proper controls do not appear to have been run. Therefore, the conclusion that PRO1114 is an inhibitory molecule appears to be premature as well as the assay not being predictive of such a conclusion.

Applicant asserts that the MLR assay is the best *in vitro* model for screening immunosuppressive agents for use in the prevention of graft-versus-host disease and graft rejection. Applicant's assertion is noted, but the assay used must be evaluated as it pertains to the asserted use of the claimed invention, which is for therapeutic enhancement of the immune response of an individual. If the claimed invention is to be used for therapeutic enhancement of the immune response of an individual, the

question to ask is how are the results of the MLR assay related to the asserted utility of the claimed invention? The Office action above goes into great depth regarding the nature of the MLR assay and how those skilled in the art use this assay and what kind of determinations can be made about compounds which are tested in this assay. The predictive nature of the MLR assay for transplantation and alloimmune response are pointed out above and support the position that the MLR assay has not been shown to be predictive for general immune responses *in vivo* because it is a special case of antigen stimulation in which T lymphocytes respond to foreign histocompatibility antigen on unrelated lymphocytes or monocytes. This reaction is not predictive of general responses of the immune system because, *in vivo*, activation of a lymphocyte is controlled not only by antigen binding but also by interactions with other cells. MLC (a.k.a. MLR) assay is a measure of alloreactivity of one individual to another individual, rather than a general measure of immune function. This reactivity is governed by the antigenic disparity between the two individuals who are being compared in the assay. Depending on the individuals being tested, the MLC may indicate stimulation if they are HLA-disparate or the MLC may indicate no stimulation if the individuals are HLA-identical. The ability of the encoded polypeptide to stimulate proliferation in the MLC assay may not be a general stimulus to lymphocyte proliferation, but rather a reaction to one of the MHC antigens on the responder cell. The instant specification fails to provide sufficient detail of the assay which was performed and fails to provide any data whatsoever in order for one of ordinary skill in the art to evaluate the conclusion that lymphocyte proliferation was stimulated by the claimed invention. As pointed out

previously, there are several controls which the art recognizes as being essential for meaningful results for this assay, including autologous controls, a control to determine maximum response, screening for possible HLA antibodies and growth support capabilities. Furthermore, there is known inherent variability of individual cellular responses from day to day, which would clearly dictate the need for internal controls. The specification indicates that CD4-IgG was used as a control, but it is not clear how this would control for background stimulation or provide for a measure of maximal stimulation. Lastly, the specification fails to provide any data or evidence of the results of the assay, therefore, one of ordinary skill in the art cannot evaluate the conclusion. The specification states that "positive increases over control are considered positive", however, this does not indicate that statistical significance must occur for determination of a positive result in the assay. In conclusion, the results of the MLC (a.k.a. MLR) assay do not support a specific and substantial utility for the claimed invention because the assay is not predictive of immune response in general, and one of ordinary skill in the art would not expect a stimulatory effect in the MLC assay to correlate to a general stimulatory effect on the immune system, absent evidence to the contrary.

Applicant cites Fung-Leung et al. for support that the MLR assay is used for identifying immunomodulatory compounds. However, the disclosure of Fung-Leung et al. is much more than what is in the instant specification and the immunosuppressive effect being measured was specifically for alloantigens. Several controls were run, as were determinations that the inhibitory effect was not related to cell toxicity. Lastly, Fung-Leung et al. concluded that the results of the multiple MLR assays and controls

"suggests its potential use as an immunosuppressant in clinical therapy" (page 364, first sentence). It was not until the compound was tested in an *in vivo* mouse model that the authors declared it an immunosuppressant. Therefore, the conclusions reached by Fung-Leung et al. are based on much more experimental data, assays and testing that that provided in the instant specification and the reference does not support the position that the MLR assay in the instant specification is predictive of the asserted use as a therapeutic compound for suppressing the immune response.

The Declaration under 37 CFR 1.132 filed 22 June 2005 is insufficient to overcome the holding of lack of utility based on results of the MLR assay. At paragraph #8 of the Declaration, Dr. Fong states "[t]he MLR assay of the present application is designed to measure the ability of a test substance to "drive" the dendritic cells to induce the proliferation of T-cells that are activated, or co-stimulated in the MLR, and thus identifies immune stimulants that can boost the immune system to respond to a particular antigen that may not have been immunologically active previously". This is not what the instant specification asserts at pages 208-209. There is no mention in the instant specification about boosting the immune system "to respond to a particular antigen that may not have been immunologically active previously". It would appear that Dr. Fong is reading the results of the Peterson et al. reference into the disclosure of the instant specification. However, the Peterson et al. reference was not available at the time the instant application was filed, therefore, reliance on the methods and results of this reference is improper.

In paragraph #9 of the Declaration, Dr. Fong states that IL-12 was first identified in an MLR in Gubler et al. (PNAS 88: 4143-4147, 1991). However, a review of Gubler et al. does not reveal the use of MLR in evaluating the biological effects of IL-12. Gubler et al. teach that IL-12 is produced by peripheral blood lymphocytes (predominantly B cells) under appropriate conditions and that IL-12 activates NK cells, facilitates the generation of specific allogeneic CTL responses and stimulates secretion of gamma-interferon. Additionally, IL-12 synergizes with IL-2 to cause the proliferation of resting peripheral blood lymphocytes. Therefore, the further work of researchers regarding IL-12 was not based on the results of a single assay, being the MLR, but rather on a body of work which provides for a number of biological activities of IL-12 which are not disclosed for the claimed invention. The claimed invention is not IL-12. Secondly, the methods of Peterson et al. are not disclosed in the instant specification and are after the filing date of the instant application.

In paragraph 10 of the Declaration, Dr. Fong asserts "a PRO polypeptide shown to stimulate T-cell proliferation in the MLR assay of the present invention with an activity of at least 180% of the control is expected to have the type of activity as that exhibited by IL-12". This is an assertion not supported by any facts or evidence of record. First, the instant specification fails to disclose the degree of activity for the claimed invention in the MLR assay. The specification states that any positive increase over control is considered positive, therefore, there is no disclosure that the activity in the assay was at least 180%. Secondly, there is no evidence of record which correlates an activity of at least 180% of control as predictive of an activity of IL-12. It is not clear from what data

this conclusion is derived. Therefore, the Declaration is not persuasive to overcome the holding of a lack of utility for the claimed invention based on the MLR assay.

Claims 58-65, 69-70, 74-77 stand rejected under 35 U.S.C. 102(e) as being anticipated by Ni et al. (Pre-grant publication U.S. 2003/0175778, published Sept. 18, 2003 with priority to June 5, 1998. A copy of Figure 1A from the provisional application is provided to establish grant of priority).

Applicant argues that they are entitled to priority to provisional application 60/087,106. This argument has been fully considered, but has not been found persuasive. The claim to priority is based on the results of the MLR assay, which has not been found to support the claimed utility of suppression of an immune response for the reasons provided above.

At page 12 of the response, Applicant presents arguments regarding a 102(a) rejection over Lal et al. However, the rejections were not made under 102(a), but rather, 102(e). Therefore, Applicant's arguments have been fully considered, but are not persuasive.

In response to Applicant's citation of *In re Stempel*, the MPEP discusses genus claims and species claims at 715.03(B):

> The principle is well established that the disclosure of a species in a cited reference is sufficient to prevent a later applicant from obtaining a "generic claim." *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989); *In re Slayter*, 276 F.2d 408. 125 USPQ 245 (CCPA 1960).
>
> Where the only pertinent disclosure in the reference or activity is a single species of the claimed genus, the applicant can overcome the rejection directly

> under 37 CFR 1.131 by showing prior possession of the species disclosed in the reference or activity. On the other hand, a reference or activity which discloses several species of the claimed genus can be overcome directly under 37 CFR 1.131 only by a showing that the applicant completed, prior to the date of the reference or activity, all of the species shown in the reference. *In re Stempel*, 241 F.2d 755, 113 USPQ 77 (CCPA 1957). Proof of prior completion of a species different from the species of the reference or activity will be sufficient to overcome a reference indirectly under 37 CFR 1.131 if the species shown in the reference or activity would have been obvious in view of the species shown to have been made by applicant. *In re Clarke*, 356, F.2d 987, 148 USPQ 665 (CCPA 1966); *In re Plumb*, 470 F.2d 1403, 176 USPQ 323 (CCPA 1973); *In re Hostettler*, 356 F.2d 562, 148 USPQ 514 (CCPA 1966).

Applicant has not demonstrated possession of the species of the reference, and therefore, the declaration filed under 37 CFR 1.131 is insufficient. Applicant was not in possession of the species of the reference and has not shown that the species of the reference would habe been obvious in view of the species shown to have been made by applicant (the species is the specific DNA molecule), and therefore, cannot overcome the reference.

Applicant's arguments regarding *In re Moore* have been fully considered, but are not persuasive especially in light of MPEP 706.02(b) and MPEP 715.07 which states "under 37 CFR 1.131 practice, proof of a utility must be shown only if the reference discloses a utility. *In re Wilkinson*, 304 F.2d 673, 134 USPQ 171 (CCPA 1962); *In re Moore*, 444 F.2d 572, 170 USPQ 260 (CCPA 1971). Where proof of utility is required, whether or not test results are required to establish the utility of the subject matter in question depends on the facts of each case. The ultimate issue is whether the evidence is such that one of ordinary skill in the art would be satisfied to a reasonable certainty that the subject matter necessary to antedate the reference possessed the alleged utility. *In re Blake*, 358 F.2d 750, 149 USPQ 217 (CCPA 1966)." Utility is

lacking in the subject matter necessary to antedate the reference, therefore, the declaration under 1.131 is insufficient.

Applicant is referred to MPEP 706.02(b) regarding overcoming a 35 U.S.C. 102 rejection based on a printed publication or patent. "When the claims of the reference U.S. patent or U.S. patent application publication and the application are directed to the same invention or are obvious variants, an affidavit or declaration under 37 CFR 1.131 is not an acceptable method of overcoming the rejection

Claim Objections

Claim 68 is objected to for depending on a rejected claim. If claim 68 were written as an independent claim (i.e. an isolated nucleic acid comprising the nucleic acid sequence of SEQ ID NO:351), the claim would be allowable.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the

shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine J. Saoud whose telephone number is 571-272-0891. The examiner can normally be reached on mttr, 8:00-2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Brenda Brumback can be reached on 571-272-0961. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

CHRISTINE J. SAOUD
PRIMARY EXAMINER

Christine J. Saoud